PATENT COOPERATION TREAT

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *day/month/year*	16 DEC 2004
Applicant's or agent's file reference 12323910/EJH/ar	IMPORTANT NOTIFICATION

International Application No.	International Filing Date	Priority Date
PCT/AU2003/001113	29 August 2003	30 August 2002

Applicant

THE CORPORATION OF THE TRUSTEES OF THE ORDER OF THE SISTERSOF MERCY IN QUEENSLAND et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translations to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide

Name and mailing address of the IPEA/AU	Authorized officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	CHRISTOPHER LUTON Telephone No. (02) 6283 2256

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
12323910/EJH/ar		
International Application No.	International Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/AU2003/001113	29 August 2003	30 August 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] C12N 5/02

Applicant

THE CORPORATION OF THE TRUSTEES OF THE ORDER OF THE SISTERSOF MERCY IN QUEENSLAND et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 6 sheet(s).

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [X] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [X] Certain observations on the international application

Date of submission of the demand	Date of completion of the report
2 March 2004	8 December 2004
Name and mailing address of the IPEA/AU	Authorized Officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	**CHRISTOPHER LUTON** Telephone No. (02) 6283 2256

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/001113

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed.

☒ the description, pages **1-23**, as originally filed,
pages , filed with the demand,
pages , received on with the letter of

☒ the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages **24-29**, received on **26 November 2004** with the letter of **26 November 2004**

☒ the drawings, pages **1/6-6/6**, as originally filed,
pages , filed with the demand,
pages , received on with the letter of

☐ the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. ☒ The amendments have resulted in the cancellation of:

☐ the description, pages

☒ the claims, Nos. **25-27**

☐ the drawings, sheets/fig.

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/001113

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be nonobvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos: **1-24 (partially)**

because: .

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☒ the claims, or said claims Nos. **1-24 (partially)** are so inadequately supported by the description that no meaningful opinion could be formed. **(See supplemental box)**

☒ no international search report has been established for said claim Nos. **1-24 (partially – see supplemental box)**

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

International application No.
PCT/AU2003/001113

V. **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims 1-24	YES
	Claims	NO
Inventive step (IS)	Claims 1-24	YES
	Claims	NO
Industrial applicability (IA)	Claims 1-24	YES
	Claims	NO

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1 - Bontkes et al.
D2 - Curti et al.
D3 - Herbst et al.

NOVELTY (N) and INVENTIVE STEP (IS) Claims 1-24

D1 discloses dendritic cells derived from $CD34^+$ cells by the use of Flt3, SCF, IL-3 and IL-6 (see abstract). D2 discloses that Flt3 and SCF are strictly required for the expansion of $CD34^+$ dendritic cell precursors. D3 discloses the use of IL-3, IL-6 and SCF to generate dendritic cells from $CD34^+$ cells.

None of D1-D3 disclose the pre-sorting of CD34+ cells into $CD33^+CD7^-CD10^-$ and $CD33^{+/-}CD7^+CD10^+$ populations prior to induction of differentiation into dendritic cells. Consequently, the claims are novel and involve an inventive step in light of D1-D3.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The claims filed 26 November 2004 include the pre-sorting of cells into a population having CD34$^{+/-}$CD7^{+}CD10^{+} markers. The specification, however, refers to the pre-sorting of cells into a population having CD33$^{+/-}$CD7^{+}CD10^{+} markers. It is not clear whether "CD34" is a typographical error for "CD33".

The claims received 26 November 2004 include the expansion of pre-sorted cells in the presence of a combination of Flt3, SCF, IL-3 and/or IL-6. It is not clear what combination are intended by the wording of this expression. For example, the expression may be construed as necessarily required Flt3, SCF and IL-3 while IL-6 is an optional component. However, the expression may also be construed in other manners.

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box III

As noted in the International Search Report, the technical features of the invention appeared to be either:

- the use of flt3-ligand, SCF, IL-3 and IL-6 in the differentiation of $CD34^+$ cells into dendritic cells, or
- the pre-sorting of $CD34^+$ cells into $CD33^+CD7^-CD10^-$ and $CD33^{+/-}CD7^+CD10^+$ populations prior to induction of differentiation into dendritic cells.

The claims were only searched to the extent that they were limited by one or other of the above concepts.

However, the claims received 26 November 2004 define the pre-sorting of cells into a population having $\underline{CD34}^{+/-}$ $CD7^+CD10^+$ markers. This subject matter was not searched. Moreover, there would not appear to be any basis in the specification for the pre-sorting of cells into a $\underline{CD34}^{+/-}CD7^+CD10^+$ population. Consequently, no opinion has been established with respect to the pre-sorting of cells into a population of $\underline{CD34}^{+/-}CD7^+CD10^+$ cells.

The claims received 26 November 2004 include the expansion of pre-sorted cells in the presence of a combination of Flt3, SCF, IL-3 and/<u>or</u> IL-6. The terminology used in the claim does not limit the claim to the use of all four of these substances. However, the International Search covered the use of <u>all four</u> of these substances in the differentiation. The use of subsets of those substances was not fully searched.

CLAIMS

1. A method for generating a population of myeloid like blood dendritic cells or lymphoid like blood dendritic cells from $CD34^+$ precursor cells said method comprising sorting said $CD34^+$ precursor cells into a population of either myeloid precursor cells characterized by the markers $CD33^+$, $CD7^-$, $CD10^-$ or a population of lymphoid precursor cells characterized by the markers $CD34^{+/-}$, $CD7^+$, $CD10^+$, culturing or expanding the myeloid or lymphoid precursor cells in the combination of Flt3, SCF, IL-3 and/or IL-6 for a time and under conditions sufficient for the myeloid precursor cells to give rise to the myeloid like blood dendritic cells characterized by being $CD11c^+$ and $CD123^-$ and the lymphoid precursor cells to give rise to lymphoid like blood dendritic cells characterized by being $CD11c^-$, $CD123^{hi}$.

2. The method of any one of Claim 1, wherein said $CD34^+$ precursor cells are isolated from a biological sample selected from the group consisting of peripheral blood, PBCMs, stem cells, monocytes, amniotic fluid, chorionic villus, cord blood, and tissue.

3. The method according to any one of Claims 1 or 2, wherein said population of $CD34^+$ precursor cells is differentiated into a specific lineage of dendritic cells selected from the group consisting of myeloid dendritic cells, lymphoid dendritic cells, Langerhans cells, interstitial dendritic cells, Afferent lymph veiled cells, blood dendritic cells and interdigitating cells.

4. The method of Claim 3, wherein said population of $CD34^+$ precursor cell is differentiated into a heterogenous population of dendritic cells.

5. The method of Claim 3, wherein said population of $CD34^+$ precursor cells is differentiated into a substantially homogenous population of dendritic cells.

6. The method of Claim 1, wherein the cytokine is selected from the group consisting of flt3, SCF, IL-3, IL-6, GM-CSF, G-CSF, TNF-α, IL-4, TNF-β, LT-β, IL-2, IL-7, IL-9, IL-15, IL-13, IL-5, IL-1α, IL-1β, IFN-γ, IL-10, IL-17, IL-16, IL-18, HGF, IL-11, MSP, FasL, TRAIL, TRANCE, LIGHT, TWEAK, CD27L, CD30L, CD40L, APRIL, TALL-1, 4-1BBL, OX40L, GITRL, IGF-I, IGF-II, HGF, MSP, FGF-a, FGF-b, FGF-3-19, NGF, BDNF, NTs, Tpo, Epo, Ang1-4, PDGF-AA, PDGF-BB, VEGF-A, VEGF-B, VEGF-C, VEGF-D, PIGF, EGF, TGF-α, AR, BTC, HRGs, HB-EGF, SMDF, OB, CT-1, CNTF, OSM, SCF, Flt-3L, M-CSF, MK and PTN or their functional, recombinant or chemical equivalents or homologues thereof.

7. The method of Claim 6, wherein the cytokine is selected from the group consisting flt3, SCF, IL-3, IL-6, GM-CSF, G-CSF, TNF-α or their functional, recombinant or chemical equivalents or homologues thereof.

8. The method of Claim 1, further comprising presenting a peptide on the surface of the dendritic cells, thereby providing a population of antigen presenting dendritic cells.

9. The method of Claim 8, wherein said antigen presenting cell is capable of activating a population of T cells.

10. The method of Claim 9, wherein said population of T cells occurs *in vitro*.

11. The method of Claim 9, wherein said population of T cells occurs *in vivo*.

12. The method of any one of Claims 9 to 11, wherein the T cell is selected from a population of $CD4^+$ T cells and/or $CD8^+$ T cells.

13. The method of Claim 9, wherein said peptide is derived from a polypeptide isolated from a human protein, a pathogen protein or a protein derived from a cancer cell.

14. The method of Claim 13, wherein said pathogen is selected from the group consisting of viruses, bacteria, fungi, ectoparasites, mycoplasms, *Archea*, algae, oomycetes, slime molds, nematodes and amoebeae.

15. The method of Claim 14, wherein said virus is selected from the group consisting of Human Immunodeficiency Virus (HIV), the human papilloma virus, Epstein-Barr virus, the polio virus, the rabies virus, the Ebola virus, the influenza virus, the encephalitis virus, smallpox virus, the rabies virus, the herpes viruses, the sendai virus, the respitory syncytial virus, the othromyxoviruses, the measles viruses, the vesicular stomatitis virus, visna virus and cytomegalovirus.

16. The method of Claim 14, wherein said fungi is selected from the group consisting of *Acremonium* spp., *Aspergillus* spp., *Basidiobolus* spp., *Bipolaris* spp., *Blastomyces dermatidis, Candida* spp., *Cladophialophora carrionii, Coccoidiodes immitis, Conidiobolus* spp., *Cryptococcus* spp., *Curvularia* spp., *Epidermophyton* spp., *Exophiala jeanselmei, Exserohilum* spp., *Fonsecaea compacta, Fonsecaea pedrosoi, Fusarium oxysporum, Fusarium solani, Geotrichum candidum, Histoplasma capsulatum* var. *capsulatum, Histoplasma capsulatum* var. *duboisii, Hortaea werneckii, Lacazia loboi, Lasiodiplodia theobromae, Leptosphaeria senegalensis, Madurella grisea, Madurella mycetomatis, Malassezia furfur, Microsporum* spp., *Neotestudina rosatii, Onychocola canadensis, Paracoccidioides brasiliensis, Phialophora verrucosa, Piedraia hortae, Piedra iahortae, Pityriasis versicolor, Pseudallesheria boydii, Pyrenochaeta romeroi, Rhizopus arrhizus, Scopulariopsis brevicaulis, Scytalidium dimidiatum, Sporothrix schenckii, Trichophyton* spp., *Trichosporon* spp., Zygomcete fungi, *Absidia corymbifera, Rhizomucor pusillus* and *Rhizopus arrhizus.*

17. The method of Claim 14, wherein is said bacteria are selected from the group consisting of *Bacillus anthracis, Bordetella pertussis, Vibrio cholerae, Escherichia coli, Shigella dysenteriae, Clostridium perfringens, Clostridium botulinum, Clostridium tetani, Corynebacterium diphtheriae, Pseudomonas aeruginosa, Bacillus anthracis, Bordetella pertussis, Staphylococcus aureus* and *Streptococcus pyogenes.*

18. The method of Claim 13, wherein said cancer cell is isolated from a cancer cell associated with a cancer selected from the group consisting of ABL1 protooncogene, AIDS Related Cancers, Acoustic Neuroma, Acute Lymphocytic Leukaemia, Acute Myeloid Leukaemia, Adenocystic carcinoma, Adrenocortical Cancer, Agnogenic myeloid metaplasia, Alopecia, Alveolar soft-part sarcoma, Anal cancer, Angiosarcoma, Aplastic Anaemia, Astrocytoma, Ataxia-telangiectasia, Basal Cell Carcinoma (Skin), Bladder Cancer, Bone Cancers, Bowel cancer, Brain Stem Glioma, Brain and CNS Tumours, Breast Cancer, CNS tumours, Carcinoid Tumours, Cervical Cancer, Childhood Brain Tumours, Childhood Cancer, Childhood Leukaemia, Childhood Soft Tissue Sarcoma, Chondrosarcoma, Choriocarcinoma, Chronic Lymphocytic Leukaemia, Chronic Myeloid Leukaemia, Colorectal Cancers, Cutaneous T-Cell Lymphoma, Dermatofibrosarcoma-protuberans, Desmoplastic-Small-Round-Cell-Tumour, Ductal Carcinoma, Endocrine Cancers, Endometrial Cancer, Ependymoma, Esophageal Cancer, Ewing's Sarcoma, Extra-Hepatic Bile Duct Cancer, Eye Cancer, Eye: Melanoma, Retinoblastoma, Fallopian Tube cancer, Fanconi Anaemia, Fibrosarcoma, Gall Bladder Cancer, Gastric Cancer, Gastrointestinal Cancers, Gastrointestinal-Carcinoid-Tumour, Genitourinary Cancers, Germ Cell Tumours, Gestational-Trophoblastic-Disease, Glioma, Gynaecological Cancers, Haematological Malignancies, Hairy Cell Leukaemia, Head and Neck Cancer, Hepatocellular Cancer, Hereditary Breast Cancer, Histiocytosis, Hodgkin's Disease, Human Papillomavirus, Hydatidiform mole, Hypercalcemia, Hypopharynx Cancer, IntraOcular Melanoma, Islet cell cancer, Kaposi's sarcoma, Kidney Cancer, Langerhan's-Cell-Histiocytosis, Laryngeal Cancer, Leiomyosarcoma, Leukaemia, Li-Fraumeni Syndrome, Lip Cancer, Liposarcoma, Liver Cancer, Lung Cancer, Lymphedema, Lymphoma, Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, Male Breast Cancer, Malignant-Rhabdoid-Tumour-of-Kidney, Medulloblastoma, Melanoma, Merkel Cell Cancer, Mesothelioma, Metastatic Cancer, Mouth Cancer, Multiple Endocrine Neoplasia, Mycosis Fungoides, Myelodysplastic Syndromes, Myeloma, Myeloproliferative Disorders, Nasal Cancer, Nasopharyngeal Cancer, Nephroblastoma, Neuroblastoma, Neurofibromatosis, Nijmegen Breakage Syndrome, Non-Melanoma Skin Cancer, Non-Small-Cell-Lung-Cancer-(NSCLC), Ocular Cancers, Oesophageal Cancer, Oral cavity

Cancer, Oropharynx Cancer, Osteosarcoma, Ostomy Ovarian Cancer, Pancreas Cancer, Paranasal Cancer, Parathyroid Cancer, Parotid Gland Cancer, Penile Cancer, Peripheral-Neuroectodermal-Tumours, Pituitary Cancer, Polycythemia vera, Prostate Cancer, Rare-cancers-and-associated-disorders, Renal Cell Carcinoma, Retinoblastoma, Rhabdomyosarcoma, Rothmund-Thomson Syndrome, Salivary Gland Cancer, Sarcoma, Schwannoma, Sezary syndrome, Skin Cancer, Small Cell Lung Cancer (SCLC), Small Intestine Cancer, Soft Tissue Sarcoma, Spinal Cord Tumours, Squamous-Cell-Carcinoma-(skin), Stomach Cancer, Synovial sarcoma, Testicular Cancer, Thymus Cancer, Thyroid Cancer, Transitional-Cell-Cancer-(bladder), Transitional-Cell-Cancer-(renal-pelvis-/-ureter), Trophoblastic Cancer, Urethral Cancer, Urinary System Cancer, Uroplakins, Uterine sarcoma, Uterus Cancer, Vaginal Cancer, Vulva Cancer, Waldenstrom's-Macroglobulinemia, Wilms' Tumour.

19. The method of Claim 13, wherein the human protein is associated with an autoimmune disease.

20. The method of Claim 19, wherein the autoimmune disease is selected from the group consisting of Addisons Disease, Allergies, Anemia, Ankylosing Spondylitis, Arthritis, Celiac Disease, Crohns Disease, Diabetes, Endometriosis, Fibromyalgia, Graves Disease, Hashimotos Disease, Hypothyroidism, Immune Diseases, Lupus, Lymphoma, Meniere's Disease, Multiple Sclerosis, Oral Diseases, Osteoporosis, Pleurisy, Psoriasis, Reiters Syndrome, Rheumatoid Arthritis, Sarcoidosis, Scleroderma, Sjogrens Syndrome, Thrush, Vitiligo, Alopecia Areata, Antiphospholipid Syndrome (APS), Behcet's Disease, Ulcerative Colitis, Goodpasture Syndrome, Graft Versus Host Disease, Guillain-Barre Syndrome, Multiple Sclerosis, Myasthenia Gravis, Myositis, Pemphigus Vulgaris, Primary Biliary Cirrhosis, Rheumatic Fever, Vasculitis and Wegener's Granulomatosis.

21. A method for inducing a protective immune response against an autoimmune disease in a subject comprising administering to said subject in need of treatment a therapeutically effective amount of a composition comprising an antigen-presenting dendritic cell generated according to Claim 19.

22. The method of Claim 19, wherein the autoimmune disease is selected from the group consisting of Addisons Disease, Allergies, Anemia, Ankylosing Spondylitis, Arthritis, Celiac Disease, Crohns Disease, Diabetes, Endometriosis, Fibromyalgia, Graves Disease, Hashimotos Disease, Hypothyroidism, Immune Diseases, Lupus, Lymphoma, Meniere's Disease, Multiple Sclerosis, Oral Diseases, Osteoporosis, Pleurisy, Psoriasis, Reiters Syndrome, Rheumatoid Arthritis, Sarcoidosis, Scleroderma, Sjogrens Syndrome, Thrush, Vitiligo, Alopecia Areata, Antiphospholipid Syndrome (APS), Behcet's Disease, Ulcerative Colitis, Goodpasture Syndrome, Graft Versus Host Disease, Guillain-Barre Syndrome, Multiple Sclerosis, Myasthenia Gravis, Myositis, Pemphigus Vulgaris, Primary Biliary Cirrhosis, Rheumatic Fever, Vasculitis and Wegener's Granulomatosis.

23. A method for inducing a protective immune response against cancer in a subject comprising administering to said subject in need of treatment a therapeutically effective amount of a composition comprising an antigen-presenting dendritic cell generated according to Claim 18.

24. A method for inducing a protective immune response against a pathogen in a subject comprising administering to said subject in need of treatment a therapeutically effective amount of a composition comprising an antigen-presenting dendritic cell generated according to any one of Claims 13 to 17.